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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,656	04/18/2005	Ralf Wilhelm Schulte	129402.00101	9867

21269 7590 01/04/2010

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EXAMINER	
HILL, KEVIN KAI	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
01/04/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,656	SCHULTE ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-20,24,26-28,31,46,48-53 and 55-58* is/are pending in the application.

4a) Of the above claim(s) *14-18 and 55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-13,19,20,24,26-28,31,46,48-53 and 56-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :July 27, 2009 and November 17, 2009.

Detailed Action

Election/Restrictions

Applicant's response to the Requirement for Restriction, filed on October 29, 2007 is acknowledged. Applicant has elected without traverse the invention designated as Invention Group II, claims 2-31 and 46, directed to a method of using a composition comprising one or more double-stranded oligoribonucleotides (dsRNA) for the specific modulation of the expression of target genes in cells and/or tissues of the CNS and/or eye, wherein said composition is introduced into a cell, tissue or organism outside the blood-brain or blood-retina barrier.

Within Group II, Applicant has further elected the restricted neural tissue subgroup, cells and tissues of the eye.

Within Group II, Applicant has elected the following species:

i) wherein the dsRNA molecule is dsRNA molecules between 21 and 23 nucleotides in length, as recited in claim 13,

ii) wherein the promoter is a tissue specific promoter, as recited in claim 20,

iii) wherein the dsRNA is complexed to a micellar structure, as recited in claim 22,

iv) wherein the means by which the dsRNA is administered to the eyeball systemic administration, as recited in claim 26,

v) wherein the eye disease is a degenerative retinal disease, as recited in claim 50, and

vi) wherein the organism is human, as recited in claim 31.

Amendments

In the reply filed September 18, 2009, Applicant has cancelled Claims 1, 21-23, 25, 29-30, 32-45, 47 and 54, withdrawn Claims 14-18 and 55, and amended Claims 2, 13 and 24, and added new claims, Claims 56-58.

Claims 14-18 and 55 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

This application contains claims drawn to an invention nonelected **without** traverse in the reply filed on October 29, 2007. Because Applicant did not distinctly and specifically point out the supposed errors in the Group or species restriction requirement, the election was treated as an election without traverse and the restriction and election requirement was deemed proper and therefore made final (MPEP §818) in the office action of January 24, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP §821.01.

Claims 2-13, 19-20, 24, 26-28, 31, 46, 48-53 and 56-58 are under consideration.

Priority

This application is a 371 of PCT/EP03/04002, filed April 16, 2003. Applicant's claim for the benefit of a prior-filed application parent provisional application 60/431,173, filed December 5, 2002, under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). While a certified copy of the foreign patent application EPO 02008671.5, filed April 18, 2002, has been filed with the instant application, a certified English translation has not been provided.

The effective priority date of the instant application is granted as April 18, 2002.

Response to Amendment

The Examiner acknowledges Applicant's filing of a translation of foreign priority documents in the papers filed September 19, 2009. While the translation document is directed to "68539-PRO/JPW/FHB", Applicant's representative states (Remarks made in Amendment, page 9) that "Applicants enclose herewith a certified translation of the present application's priority document". Thus, on its face, the Examiner considers the translation document directed to "68539-PRO/JPW/FHB" to be a certified translation of foreign priority document EPO 02008671.5.

Information Disclosure Statement

Applicant has filed Information Disclosure Statements on July 27, 2009 and November 17, 2009 that have been considered.

The signed and initialed PTO Forms 1449 are mailed with this action.

Examiner's Note

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the September 18, 2009 response will be addressed to the extent that they apply to current rejection(s).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

1. **The prior objection to Claims 2, 13 and 24 are withdrawn** in light of Applicant's amendment to the claims.

Claim Rejections - 35 USC § 102

2. **The prior rejection of Claims 2, 5, 7-13, 24, 26-28, 31 and 50 under 35 U.S.C. 102(b)** as being anticipated by Carter (U.S. Patent No. 5,712,257), as evidenced by Rummelt et al (Opthalmology 101(2):270-279, 1994; Abstract only) **is withdrawn** in light of Applicant's amendment to the claims to recite the first and second strands of the dsRNA molecule are complementary to each other, a limitation that Carter does not teach.

3. **Claims 2-13, 19-20, 24, 26-28, 31, 46, 48 and 50 stand and Claim 56-58 are newly rejected under 35 U.S.C. 102(a) and 35.U.S.C 102(e)** as being anticipated by King (U.S. 2002/0165158 A1), as evidenced by Caplen (Trends in Biotech. 20(2):49-51, 2002).

With respect to Claim 56, King discloses the pharmaceutical composition may be administered parenterally, i.e. intravenously [0125, 0184, 0187].

With respect to Claims 57-58, for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase 'consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1240-41, 68 USPQ2d 1280, 1283-84 (Fed. Cir. 2003) (Applicant's statement in the specification that "silicon contents in the coating metal should not exceed about 0.5% by weight" along with a discussion of the deleterious effects of silicon provided basis to conclude that silicon in excess of 0.5% by weight would materially alter the basic and novel properties of the invention. Thus, "consisting essentially of" as recited in the preamble was interpreted to permit no more than 0.5% by weight of silicon in the aluminum coating.); *In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. *In re De Lajarte*, 337 F.2d 870, 143 USPQ

256 (CCPA 1964). See also *Ex parte Hoffman*, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although 'consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by 'consisting essentially of' language."). In the instant case, the transitional phrase "consisting essentially of", i.e. "a composition consisting essentially of" (Claim 57), is interpreted to be equivalent to the transitional phrase "comprising", i.e. "a composition comprising" (Claim 2). King discloses the nucleic acids of the invention, i.e. dsRNA [0128], may be combined with one or more suitable carriers [0126] appropriate for the route of administration [0184], wherein the carrier may be a saline [0187].

Response to Arguments

Applicant argues that the Office's interpretation of the term "naked" and "comprising" is incorrect, more specifically, that the disclosure that the dsRNA can be delivered with other carriers, i.e. liposomes, should not be construed as "encapsulating naked dsRNA molecules". If a dsRNA is encapsulated, then it is not naked.

Applicant's argument(s) has been fully considered, but is not persuasive.

As a first matter, the specification discloses that a preferred embodiment of the method is to administer the pharmaceutical composition comprising a naked dsRNA by a suitable carrier (pg 14, lines 1-5), whereby "such a carrier can be a micellar structure, preferably a liposome" (pg 13, lines 4-5). The Examiner notes that the working examples fail to disclose the carrier used to administer the dsRNA molecules with which Applicant achieved the post-transcriptional gene silencing. Thus, in light of the disclosure, the broadest reasonable interpretation of the instant claims reasonably embraces "a composition comprising" a carrier vehicle, e.g. micelle or liposome, encapsulating naked dsRNA molecules.

As a second matter, Applicant appears to have overlooked that King discloses the nucleic acids of the invention, i.e. dsRNA [0128], may be combined with one or more suitable carriers

[0126] appropriate for the route of administration [0184], wherein the carrier may be a saline [0187].

Applicant argues that King does not teach the first and second strands of the dsRNA molecule to be complementary to each other.

Applicant's argument(s) has been fully considered, but is not persuasive. While King does not disclose *ipsis verbis* the first and second strands of the dsRNA molecule to be complementary to each other, Applicant appears to have overlooked that King cites [0129] Elbashir et al (Nature 411(6836):494-498, 2001) who teaches the gene-silencing effects of dsRNA in which the first and second strands of the dsRNA molecule to be complementary to each other (Figure 1). Thus, at the time of the instantly claimed invention, those of ordinary skill in the art would have understood the King disclosure to read upon dsRNA molecules in which the first and second strands of the dsRNA molecule are complementary to each other.

4. **The prior rejection of Claims 2, 5-10, 13, 19-20, 24, 26-28, 31 and 48-53 stand and under 35 U.S.C. 102(e)** as being anticipated by Tolentino et al (U.S. Patent No. 7,148,342 B2) **is withdrawn** in light of Applicant's filing of a certified translation of the foreign priority document EPO 02008671.5. Thus, Tolentino et al is no longer considered prior art.

Claim Rejections - 35 USC § 103

5. **Claims 2-13, 19-20, 24, 26-28, 31, 46 and 48-53 stand, and Claims 56-58 are newly rejected under 35 U.S.C. 103(a)** as being unpatentable over Robinson et al (U.S. Patent No. 5,814,620) in view of LaFleur et al (U.S. 6,433,145 B1) and Tuschl et al (U.S. 2002/0086356 A1).

Response to Arguments

Applicant argues that the combination of references fail to yield a composition comprising naked dsRNA. The Office's interpretation of the term "naked" and "comprising" is incorrect, more specifically, that the disclosure that the dsRNA can be delivered with other carriers, i.e. liposomes, should not be construed as "encapsulating naked dsRNA molecules". If a dsRNA is encapsulated, then it is not naked.

Applicant's argument(s) has been fully considered, but is not persuasive.

As a first matter, the specification discloses that a preferred embodiment of the method is to administer the pharmaceutical composition comprising a naked dsRNA by a suitable carrier (pg 14, lines 1-5), whereby "such a carrier can be a micellar structure, preferably a liposome" (pg 13, lines 4-5). The Examiner notes that the working examples fail to disclose the carrier used to administer the dsRNA molecules with which Applicant achieved the post-transcriptional gene silencing. Thus, in light of the disclosure, the broadest reasonable interpretation of the instant claims reasonably embraces "a composition comprising" a carrier vehicle, e.g. micelle or liposome, encapsulating naked dsRNA molecules.

As a second matter, Applicant appears to have overlooked that Robinson et al disclose the oligonucleotides may be formulated with a pharmaceutically acceptable carrier well known in the art (col. 8, lines 54-61), i.e. physiological saline (col. 10, lines 11-12), and disclose formulating a composition consisting essentially of a gene-silencing oligonucleotide and phosphate-buffered saline (Example 2) or a balanced salt solution (Example 3). Similarly, LaFleur et al also discloses administering intravenously (col. 78, lines 61-63; col. 102, lines 52-55) naked polynucleotides with an aqueous carrier (col. 101, lines 33-40), whereby the aqueous carrier may be saline (col. 181, lines 52-55). Thus, at the time of the instantly asserted invention, it was routine for those of ordinary skill in the art to formulate a composition consisting essentially of a dsRNA molecule and saline.

Applicant argues that the Office has failed to show that one of skill in the art would have had a reasonable expectation of success performing the claimed method with naked dsRNA, as there is no indication that naked dsRNA can even cross the blood-brain or blood-retina barrier.

Applicant's argument(s) has been fully considered, but is not persuasive. Applicant appears to have overlooked that Robinson et al disclose that in diseases concerning blood vessels, e.g. diabetic retinopathy, the vessels are abnormal and leaky, and thus the problem of passage through the blood brain barrier may not be a problem. Therefore, systemic delivery, i.e. intravenous injection (col. 9, line 65), may prove efficacious (col. 11, lines 15-19). Thus, at the time of the instantly asserted invention, those of ordinary skill in the art possessed a reasonable

expectation of success that naked dsRNA could cross the blood-brain or blood-retina barrier when administered parenterally to an organism.

Conclusion

6. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/
Examiner, Art Unit 1633